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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,038	07/28/2005	Harold C Smith	21108.0034U2	6473

23859 7590 10/27/2008

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
10/27/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,038	SMITH ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-98,101-105,107-117 and 121-127* is/are pending in the application.

4a) Of the above claim(s) *1-97,111-117 and 121-124* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *98,101-105,107-110 and 125-127* is/are rejected.

7)☒ Claim(s) *105 and 125* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed 15 July 2008. Claims 99, 100, 106, and 118-120 have been cancelled. Claims 125-127 have been added. Claims 1-98, 101-105, 107-117 and 121-127 are pending. Claims 1-97, 111-117 and 121-124 are drawn to a nonelected subject matter and hence are withdrawn from further consideration pursuant to 37 CFR 1.142(b). Claims 98, 101-105, 107-110 and 125-127 are currently examined.

Claim Objections

The objection to claims 105 and 118 is **withdrawn** in response to Applicant's amendment.

Claim 105 is objected to for failing to define the acronym "AID" at the first occurrence in the claims. Applicant may consider amending the claims to read --- comprising the deaminase, activation-induced cytidine deaminase (AID), --- at line 5 of the claim for clarity.

New claim 125 is objected to because the first line is missing a space between "98" and the word "or."

Response to Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 98-104 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is **withdrawn** in response to Applicants' amendment.

The rejection of claims 105 and 107-110 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement is **maintained and extended to new claims 125-127**.

Claims 105-110 and 125-127 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. §112 ¶ 1, the courts have put forth a series of factors (MPEP §2164.01(a)). See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative

skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The nature of the invention is *ex vivo* antibody induction in B cells with a viral RNA- editing deaminase, activation-induced cytidine deaminase (AID), fused to a protein transduction domain and the induced B cell therapy for the treatment of hyper-IgM syndrome. The claims encompass all kinds of immune responses including the production of IgG, IgA, and IgE. The breadth of the claimed invention is exceedingly large and fails to receive adequate support in the specification. The disclosure fails to provide adequate guidance pertaining to a number of considerations as follows:

The disclosure fails to provide any working embodiments that meet the claimed limitations. While there are examples that characterize the structures and functions of various deaminases, namely CEM15, ARP1, Cddl, AID, APOBEC1 and its related proteins by structural comparison and activity assays and methods for identifying inhibitors, they do not relate to contacting B lymphocytes *ex vivo* and measuring the amount of IgE, IgA and IgG produced in the B cells, let alone the treatment of hyper-lgM syndrome. No *in vivo* working example of B cell therapy for the treatment of hyper-IgM syndrome is disclosed in the specification.

The specification provides little guidance regarding practice of the claimed methods. 1) One skilled in the art is left with no guidance on how to target the chimeric protein to only B lymphocyte cells in the subject body. 2) The disclosure fails to provide

sufficient guidance pertaining to the underlying cellular mechanisms in the treatment of hyper-IgM syndrome with B cell induction. The specification does not disclose the effect, if any, of the deaminase-contacted B lymphocyte cells in a diseased or normal model. 3) The disclosure also fails to provide any guidance pertaining to the molecular determinants of the RNA-editing deaminase, AID, that are involved in the induction of immune response, which might enable the skilled artisan rationally identify the "functional fragment or derivative" that functions in the claimed manner. However, without sufficient guidance pertaining to a suitable molecular target, the skilled artisan has only been extended an undue invitation to further experimentation to ascertain or identify which "fragment or derivative" might function in the desired manner. 4) Furthermore, there is no teaching of the specificity, type, and duration of the immune response.

The prior art is unpredictable and fails to provide sufficient illumination pertaining to the structural constraints governing B-cell targeted delivery of AID and the cellular or molecular mechanisms underlying the treatment of the hyper-IgM syndrome. However, no such guidance is available in the specification for the treatment of hyper-IgM syndrome with viral RNA-editing AID. Although the activation-induced cytidine deaminase (AID) is known to induce antibody protein production in B lymphocyte cells *in vitro* by involving in the somatic hypermutation of the variable regions in the immunoglobulins (Martin et al., 2002), the clinical efficacy of the AID-induced B lymphocyte replacement therapy is unknown and undeveloped.

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). See M.P.E.P. §2164.03 [R-2]. Relationship of Predictability of the Art and the Enablement Requirement. Lacking the knowledge in the state of the art as well as the predictability in the art of treatment of hyper-IgM syndrome by *ex vivo* B cell induction, one skilled in the art is only left with the specification of instant application for guidance to the practice the claimed method. However, the instant specification nowhere provides a description or working example of the claimed method of treating a subject for hyper-IgM syndrome.

"Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See *Fields v, Conover*, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). The disclosure fails to provide sufficient working embodiments to enable the breadth of the claimed invention. Legal precedence dictates that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C 1991). *In re Angstadt*, 537 F.2d 498,502-03, 190 U.S.P.Q. 214, 21 (C.C.P.A. 1976). In regards to the deaminase, this is pure speculation on Applicant's part that AID can treat a somatic hypermutation disorder like hyper-IgM syndrome in a subject, especially in humans, given that the state of the art of "deaminase-induced B cell therapy" is undeveloped. There is no specific guidance in

the art or specification and no specific examples of treatment set forth in the specification. While Applicant is not required to set forth working examples, the specification must set forth sufficient teachings to allow one to practice the claimed invention. There is no evidence that the claimed AID-induced B cell therapy will actually be suitable for treating hyper-IgM syndrome. When all the aforementioned factors are considered in toto, it would clearly require undue and unpredictable experimentation from the skilled artisan to practice the claimed invention.

Thus, the instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

Applicant's amendment to the claims has been fully considered but the instant claims are not supported by the specification for the reasons set forth above. Applicant did not present any arguments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 98 and 101-104 under 35 U.S.C. §103(a) as being obvious over Martin *et al.* (2002, No. A227 in the IDS filed on 08 December 2005) in

view of Schwarze *et al.* (2000, No. A305 in the IDS filed on 08 December 2005) and Sutkowski *et al.* (1994) **is maintained and extended to new claims 125 and 126.**

The instant claims are drawn to a method of inducing an immune response to an antigen in a subject comprising contacting a B lymphocyte cell *ex vivo* with a chimeric protein comprising a protein transduction domain and a deaminase domain comprising AID, and thereby induce antibody production in the B lymphocyte cell to afford a stronger immune response to an antigen in the subject.

Martin *et al.* disclose contacting three human B cell lines, Ramos, BL-2 and CL-01, respectively, with vectors expressing human activation-induced cytidine deaminase (AID). AID is expressed specifically in germinal-center centroblasts of a B lymphocyte cell during B cell differentiation and is required for somatic hypermutation of the immunoglobulin variable region genes, the process which produces high affinity protective antibodies. See page 802, 2nd column. Martin *et al.* disclose that hybridomas (antigen-challenged B cells fused with myeloma tumor cells that can grow indefinitely in culture) can be induced to undergo high rates of somatic hypermutation with expression of AID to obtain subclones that produce high-affinity monoclonal antibodies and/or antibodies that are more specific. See page 805, 1st column, first full paragraph.

Martin *et al.* do not disclose contacting a B lymphocyte cell with the chimeric protein comprising a deaminase and a protein transduction domain.

Schwarze *et al.* suggest covalently tethering pharmacological proteins, compounds, or DNA to protein transduction domains (PTD), which possess the ability to cross the lipid bilayer of cells in a concentration-dependent manner, to deliver these molecules to all cells *in vivo*. See page 45, the sentence bridging the 1st and the 2nd column. Schwarze *et al.* specifically disclose the Tat transduction domain. See page 45, 3rd column, and Figure 1. Schwarze *et al.* specifically disclose protocols for Tat fusion proteins to transduce into cells and yield biological activity. See page 46, 3rd column.

Neither Martin *et al.* or Schwarze *et al.* disclose introducing the protein-contacted B lymphocyte cells into the subject.

However, Sutkowski *et al.* disclose injecting deaminase-expressing B lymphocyte cells into mice intravenously. See page 8876.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the B cell antibody induction method of Martin et al. so as to replace the vector expression of AID with a direct cell delivery by fusing AID with Tat PTD as taught by Schwarze *et al.* The skilled artisan would have been motivated to do so to improve the contact between the B lymphocyte cell and AID. It would also have been obvious to modify the method of Martin *et al.* so as to include a further step to introduce the B lymphocyte cells into the subject after they are contacted with the therapeutic deaminase, as taught by Sutkowski *et al.* There would have been a reasonable expectation of success, given it is known in the art that Tat PTD fusion

proteins can transduce different proteins into all cell types and yield biological activity, as taught by Schwarze *et al.*, and given that it is long been known in the art to contact B lymphocyte cells with a therapeutic protein *ex vivo* and subsequently introduce the B cells into the subject, as shown by Sutkowski *et al.* Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed on 15 July 2008 have been fully considered but are not persuasive. Applicant argues that the method taught by Martin *et al.* of expressing the AID molecule *in vitro* is very different than the claimed method of contacting a B lymphocyte cell *ex vivo* with a chimeric protein comprising AID, and one skilled in the art would not know whether AID retains its function when coupled to Tat based on the teachings of Schwarze *et al.* and Martin *et al.*

In response to Applicant's argument about the differences between the claimed invention and the prior art, Examiner presents the following facts: First of all, the claim term "*ex vivo*" means outside of a living organism, which encompasses the prior art term "*in vitro*" that means in a laboratory vessel. Secondly, although Martin *et al.* teach expressing the AID protein by contacting B lymphocyte cells with vectors expressing AID rather the claimed method step of directly contacting the chimeric protein with the B cells, the end result of the Martin method step remains the same as the claimed step,

which is to present the chimeric protein as an antigen to the B lymphocyte cell to produce antibodies. The different approaches to delivering the chimeric protein to the inside of the cells do not materially affect the end result of inducing antibody production in the B lymphocyte cell. Applicant conceded that Martin *et al.* disclose producing high-affinity monoclonal antibodies and/or more specific antibodies with antigen-challenged B cells. Thirdly, Applicant's argument, AID expression leading to somatic hypermutation is vastly different from inducing an immune response in a subject by subjecting the cells *ex vivo* to a chimeric protein, is mischaracterizing the rejection and disregarding the third reference, Sutkowski *et al.*, which discloses inducing an immune response in a mouse subject by subjecting the cells *ex vivo* to a deaminase. Examiner agrees that Martin *et al.* does not disclose inducing an immune response in a subject. However, Martin *et al.* describes inducing the B cells *ex vivo*, or more specifically, *in vitro*, with AID by vector expression, while Sutkowski *et al.* disclose inducing immune response to an antigen in a subject comprising administering a deaminase-induced B cell to the subject.

Applicant argues that Schwarze *et al.* does not show that Tat fusion proteins can transduce different proteins into all cell types and yield biological activity. However, this sentence is quoted directly from the cited publication by Schwarze *et al.* Applicant has expressed a strong opinion with doubt about the ability of Tat fusion proteins to transduce different proteins into all cell types and yield biological activity, yet Applicant does not present any evidence to show the alleged unpredictability of Tat-deaminase

fusion proteins. According to the MPEP, evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). See also *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-08, 18 USPQ2d 1016, 1022-23 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). In this case, Applicant has not provided any evidence to support the argument that no immune response could have been elicited in a subject by coupling Tat to AID and contacting it *ex vivo* with B cell for expansion before introducing to a subject. Applicant asserts that no combination of the art and/or the knowledge generally available to those of skill in the art at the time the application was filed provides a reasonable expectation of success. However, Applicant's assertion lacks evidentiary basis. The rationale of the rejection at issue clearly sets forth the elements from the teachings in prior art that would lead to a reasonable expectation of success with the combination of the Martin and Schwarze references to arrive at the claimed invention.

To be of probative value, any objective evidence should be supported by actual proof. Due to the absence of tests comparing applicant's AID-Tat or Tat-AID fusion proteins with those of the closest prior art, the Examiner concludes that applicant's assertions of unexpected results of Tat fusion proteins are mere argument. See MPEP §716.01(b). A showing of unexpected results must be based on evidence, not argument or speculation. *In re Mayne*, 104 F.3d 1339, 1343-44, 41 USPQ2d 1451, 1455-56 (Fed. Cir. 1997) (conclusory statements that claimed compound possesses

unusually low immune response or unexpected biological activity that is unsupported by comparative data held insufficient to overcome *prima facie* case of obviousness). The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See MPEP §2145.

New Claim Rejections - 35 USC § 103 – Necessitated by Amendment

Claim 127 is rejected under 35 U.S.C. §103(a) as being unpatentable over Martin *et al.* (2002, No. A227 in the IDS filed on 08 December 2005) in view of Schwarze *et al.* (2000, No. A305 in the IDS filed on 08 December 2005), Yang *et al.* (1997, No. A389 in the IDS filed on 08 December 2005) and Sutkowski *et al.* (1994).

The instant claims are drawn to a method of inducing an immune response to an antigen in a subject comprising contacting a B lymphocyte cell *ex vivo* with a chimeric protein comprising a protein transduction domain and a deaminase domain comprising AID, and thereby induce antibody production in the B lymphocyte cell to afford a stronger immune response to an antigen in the subject.

Martin *et al.* disclose contacting three human B cell lines, Ramos, BL-2 and CL-01, respectively, with vectors expressing human activation-induced cytidine deaminase

(AID). AID is expressed specifically in germinal-center centroblasts of a B lymphocyte cell during B cell differentiation and is required for somatic hypermutation of the immunoglobulin variable region genes, the process which produces high affinity protective antibodies. See page 802, 2nd column. Martin *et al.* disclose that hybridomas (antigen-challenged B cells fused with myeloma tumor cells that can grow indefinitely in culture) can be induced to undergo high rates of somatic hypermutation with expression of AID to obtain subclones that produce high-affinity monoclonal antibodies and/or antibodies that are more specific. See page 805, 1st column, first full paragraph.

Martin *et al.* do not disclose contacting a B lymphocyte cell with a chimeric protein comprising a deaminase and a protein transduction domain, and further comprising a cytoplasmic localization protein or a fragment thereof.

Yang *et al.* disclose a chimeric protein of RNA-editing deaminase APOBEC-1 fused to CMPK, APOBEC-1-CMPK, from N-to C-terminus (page 13075, Materials and Methods, Plasmids) and that CMPK functions as a cytoplasmic localization protein. See page 13077, right column.

Yang *et al.* do not disclose the protein transduction domain in the chimeric protein.

Schwarze *et al.* suggest covalently tethering pharmacological proteins, compounds, or DNA to protein transduction domains (PTD), which possess the ability to cross the lipid bilayer of cells in a concentration-dependent manner, to deliver these

molecules to all cells *in vivo*. See page 45, the sentence bridging the 1st and the 2nd column. Schwarze *et al.* specifically disclose the Tat transduction domain. See page 45, 3rd column, and Figure 1. Schwarze *et al.* specifically disclose protocols for Tat fusion proteins to transduce into cells and yield biological activity. See page 46, 3rd column.

None of Martin *et al.*, Yang *et al.*, and Schwarze *et al.* disclose introducing the protein-contacted B lymphocyte cells into the subject.

However, Sutkowski *et al.* disclose injecting deaminase-expressing B lymphocyte cells into mice intravenously. See page 8876.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the B cell antibody induction method of Martin *et al.* so as to replace the vector expression of AID with a direct cell delivery by fusing AID with Tat PTD as taught by Schwarze *et al.* The skilled artisan would have been motivated to do so to improve the contact with the B lymphocyte cell and AID expression. It would have been obvious to modify the method of Martin *et al.* so as to include a third polypeptide comprising a cytoplasmic localization protein fused to the deaminase, for the purpose of enhancing localization of the chimeric protein to the cytoplasm, as taught by Yang *et al.* It would also have been obvious to modify the method of Martin *et al.* so as to include a further step to introduce the B lymphocyte cells into the subject after they are contacted with the therapeutic deaminase, as taught by Sutkowski *et al.* There would have been a reasonable expectation of success, given it is known in the art

that Tat PTD fusion proteins can transduce different proteins into all cell types and yield biological activity, as taught by Schwarze *et al.*, and given that it is long been known in the art to contact B lymphocyte cells with a therapeutic protein *ex vivo* and subsequently introduce the B cells into the subject, as shown by Sutkowski *et al.* Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648
15 October 2008
/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648